

support.

I. 1994. 02
Claim 2 (amended) A pharmaceutical composition according to claim 1, containing, as active ingredient, a NO synthase inhibitory substance and a metabolic antioxidant substance.

How does this differ from prior art clm. 1?
doesn't further limit clm. 1
Claim 3 (amended) A pharmaceutical composition of claim 1 wherein the NO synthase inhibitory substance and the metabolic antioxidant substance are in separated form. *sp.* *(D)*

I. 1994. 02
Claim 4 (amended) A pharmaceutical composition of claim 1 wherein the metabolic antioxidant is selected from the group consisting of dithiothreitol, pyritinol, lipoic acid and its derivatives, the dimeric disulfide derivatives of penicillamine or N-acetylcysteine, and peptides comprising at least two cysteine residues. *sp.* *(D)*

Claim 5 (amended) A pharmaceutical composition of claim 1 wherein the NO synthase inhibitory substance and the metabolic antioxidant substance are in the form of a salt.

Claim 6 (amended) A pharmaceutical composition of claim 5, wherein the salt is formed from a derivative of the NO synthase inhibitory substance containing at least one basic group and a derivative of the metabolic antioxidant substance containing at least one acid group.

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Claim 7 (amended) A pharmaceutical composition of claim 5 wherein the metabolic antioxidant is selected from the group consisting of lipoic acid or its derivatives, the dimeric disulfide derivatives of penicillamine or N-acetylcysteine and peptides containing at least two cysteine residues.

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Claim 8 (amended) A pharmaceutical composition of claim 1 wherein the NO synthase inhibitor is selected from the group consisting of a compound of amino acid type, a compound of the guanidine isothiurea, nitro- and cyano-aryl, amino-pyridine, amino-pyrimidine, amidine, indazole and imidazole families.

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Claim 9 (amended) A pharmaceutical composition of claim 8 wherein the NO synthase inhibitor of amino-acid type selected from the group consisting of is L-arginine, ornithine and lysine derivatives.

Claim 10 (amended) A pharmaceutical composition of claim 1 wherein the NO synthase inhibitor is selected from the group consisting of L-nitro-arginine, L-nitro-arginine methyl ester, L-N-monomethylarginine, aminoguanidine, agmatine, 2-amino-1-(methylamino)benzimidazole, 5-nitro-indazole, 6-nitro-indazole, 7-nitro-indazole, 1,2-(trifluoromethylphenyl) imidazole, 2-amino-4-methyl-6-(2-aminoethyl)pyridine, 2-iminopiperidine, 2-iminohomopiperidine, 2-imino-5,6-dihydro-1,3-thiazine, 2-imino-5,6-dihydro-1,3-oxazine, 2-iminotetrahydropyrimidine, N-phenyl-2-

deleted

thiophenecarboximidamine, S-ethylisothiurea,

S-methyl-L-

thiocitrulline and S-ethyl-L-thiocitrulline.

I.
Con't. Claim 11 (amended) A pharmaceutical composition of claim 1 wherein the metabolic antioxidant is lipoic acid in racemic or enantiomeric form.

Claim 12 (amended) A pharmaceutical composition of claim 1 wherein the NO synthase inhibitor is a neuronal and/or inducible NO synthase inhibitor.

Cancel claims 13 to 24 and add the following claims.

III
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--25. A method of treating pathologies in warm-blooded animals wherein nitrogen monoxide and redox status of the thiol groups are involved comprising administering to warm-blooded animals in need thereof a sufficient amount of a composition of claim 1 sufficient to treat said pathologies.

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26. A method of treating a pathology selected from the group consisting of cardiovascular and cerebrovascular disorders, septic shock, radioactive irradiation, solar radiation, organ transplants, disorders of the central or peripheral nervous system and more particularly Parkinson's' disease, proliferative and inflammatory diseases, autoimmune and viral diseases, diabetes and its complications, autosomal genetic diseases and pathologies

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characterized by a production or a dysfunction of nitrogen monoxide and/or involving the redox status of thiol groups in warm-blooded animals comprising administering to warm-blooded animals in need thereof a sufficient amount of a composition of claim 1 to treat said pathology. SP.

IV
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Claim 27 (amended) The method of claim 26 wherein the pathology is selected from the group consisting of migraine, arterial hypertension, cardiac or cerebral infarctions of ischemic or hemorrhagic origin, ischemias and thromboses. SP.

Claim 28 (amended) The method of claim 26 wherein the pathology is selected from the group consisting of migraine, arterial hypertension, cardiac or cerebral infarctions of ischemic or hemorrhagic origin, ischemias and thromboses, neurodegenerative diseases, and more particularly Parkinsons's disease, pain, cerebral or bone marrow traumas, addiction to opiates, alcohol and addictive substances, erectile and reproductive disorders, cognitive disorders, encephalopathies, depression, anxiety, schizophrenia, epilepsy, sleeping disorders and eating disorders. SP.

Claim 29 (amended) The method of claim 26 wherein the pathology is selected from the group consisting of migraine, arterial hypertension, cardiac or cerebral infarctions of ischemic or hemorrhagic origin, ischemias and thromboses, neurodegenerative diseases, and more particularly Parkinsons's disease, pain, SP.

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cerebral or bone marrow traumas, addiction to opiates, alcohol and
addictive substances, erective and reproductive disorders,
cognitive disorders, encephalopathies, depression, anxiety,
schizophrenia, epilepsy, sleeping disorders and eating disorders,
lupus, AIDS, parasitic and viral infections, diabetes and its
complications including retinopathies, nephropathies and
polyneuropathies, multiple sclerosis and myopathies.

IV
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Claim 30 (amended) The method of claim 26 wherein the
pathology is selected from the group consisting of migraine,
arterial hypertension, cardiac or cerebral infarctions of ischemic
or hemorrhagic origin, ischemias and thromboses, neurodegenerative
diseases, and more particularly Parkinsons's disease, pain,
cerebral or bone marrow traumas, addiction to opiates, alcohol and
addictive substances, erective and reproductive disorders,
cognitive disorders, encephalopathies, depression, anxiety,
schizophrenia, epilepsy, sleeping disorders and eating disorders,
lupus, AIDS, parasitic and viral infections, diabetes and its
complications including retinopathies, nephropathies and
polyneuropathies, multiple sclerosis and myopathies, cancer,
atherosclerosis, pulmonary hypertension, glomerulonephritis, portal
hypertension, cataracts, psoriasis, arthrosis and rheumatoid
arthritis, fibroses, amyloidoses and inflammations of the
gastrointestinal system and the pulmonary system and airways. P

III
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Claim 31 (amended) The method of claim 25 wherein the NO

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synthase inhibitor is selected from the group consisting of a compound of amino acid type and a compound of the guanidine, isothioureia, nitro- or cyano-aryl, amino-pyridine or amino-pyrimidine, amidine, indazole or imidazole families.

III.
Cont.
Claim 32 (amended) The method of claim 31 wherein the NO synthase inhibitor is selected from the group consisting of L-arginine, ornithine and lysine derivatives.

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Claim 33 (amended) The method of claim 25 wherein NO synthase inhibitor is selected from the group consisting of L-nitro-arginine, L-nitro-arginine methyl ester, L-N-monomethylarginine, aminoguanidine, agmatine, 2-amino-1-(methylamino)benzimidazole, 5-nitro-indazole, 6-nitro-indazole, 7-nitro-indazole, 1,2-(trifluoromethylphenyl) imidazole, 2-amino-4-methyl-6-(2-aminoethyl)pyridine, 2-iminopiperidine, 2-iminohomopiperidine, 2-imino-5,6-dihydro-1,3-thiazine, 2-imino-5,6-dihydro-1,3-oxazine, 2-iminotetrahydropyrimidine, N-phenyl-2-thiophenecarboximidamine, S-ethylisothioureia, S-methyl-L-thiocitrulline and S-ethyl-L-thiocitrulline.

Claim 34 (amended) The method of claim 25 wherein the metabolic antioxidant is selected from the group consisting of dithiothreitol, pyritinol acid or its derivatives, the dimeric disulfide derivatives of penicillamine or N-acetylcysteine and peptides comprising at least two cysteine residues.